WO 2005/023199 PCT/US2004/029037

## WHAT IS CLAIMED IS:

i

| 1 | 1. A method of detecting cancer in a patient, the method comprising:                    |  |  |
|---|---|--|--|
| 2 | determining the level of a transcript encoding SEQ ID NO:2 in a biological              |  |  |
| 3 | sample from the patient; and  |  |  |
| 4 | detecting a decrease in the level of the transcript relative to normal, thereby         |  |  |
| 5 | detecting the presence of cancer in the patient.  |  |  |
| 1 | 2 The mothed of claims 1 miles in the course is selected from a course                  |  |  |
| 1 | 2. The method of claim 1, wherein the cancer is selected from a group                   |  |  |
| 2 | consisting of lung cancer, breast cancer, mesothelioma, colon cancer, and sarcoma.      |  |  |
| 1 | 3. The method of claim 1, wherein the step of determining the level of the              |  |  |
| 2 | transcript comprises an amplification reaction.   |  |  |
| _ |   |  |  |
| 1 | 4. A method of detecting cancer in a patient, the method comprising:                    |  |  |
| 2 | determining the level of a polypeptide having the sequence set forth in SEQ             |  |  |
| 3 | ID NO:2 in a biological sample from the patient: and                                    |  |  |
| 4 | detecting an increase in the level of the polypeptide relative to normal, thereby       |  |  |
| 5 | detecting the presence of cancer in the patient.  |  |  |
| 1 | 5. The method of claim 4, wherein the cancer is selected from the group                 |  |  |
| 2 | consisting of lung cancer, breast cancer, mesothelioma, colon cancer, and sarcoma.      |  |  |
| _ | consisting of rang cancer, oreast cancer, mesomenoma, colon cancer, and sarcoma.        |  |  |
| 1 | 6. The method of claim 4, wherein the step of determining the level of the              |  |  |
| 2 | polypeptide comprises performing an immunoassay.  |  |  |
| 1 |   |  |  |
| 1 | 7. A method of detecting cancer in a patient, the method comprising:                    |  |  |
| 2 | determining the amount of methylation of a SOCS-3 promoter in a biological              |  |  |
| 3 | sample from the patient; and  |  |  |
| 4 | detecting an increase in the amount of methylation of the sample relative to            |  |  |
| 5 | normal, thereby detecting the presence of cancer in the patient.                        |  |  |
| 1 | 8. The method of claim 7, wherein the amount of methylation of the CpG                  |  |  |
| 2 | residues that occur within the region from -1005 to -983 or from -754 to -737 of SEQ ID |  |  |
| 3 | NO:3 is determined.   |  |  |
|   |   |  |  |

WO 2005/023199 PCT/US2004/029037

| 1 | 9. The method of claim 7, wherein the amount of methylation of the                         |  |  |
|---|--|--|--|
| 2 | SOCS-3 promoter is determined using bisulfite sequencing.                                  |  |  |
| 1 | 10. The method of claim 7, wherein the amount of methylation of the                        |  |  |
| 2 | SOCS-3 promoter is determined using methylation-specific PCR.                              |  |  |
| 1 | 11. The method of claim 7, wherein the amount of methylation is detected                   |  |  |
| 2 | using a methylation-sensitive restriction enzyme.  |  |  |
| 1 | 12. A method of monitoring the efficacy of a therapeutic treatment of                      |  |  |
| 2 | cancer, the method comprising the steps of:  |  |  |
| 3 | (i) providing a biological sample from a patient undergoing the therapeutic                |  |  |
| 4 | treatment; and   |  |  |
| 5 | (ii) detecting the level of: a polypeptide having an amino acid sequence of                |  |  |
| 6 | SEQ ID NO:2, or of a nucleic acid that encodes the polypeptide, in the biological sample   |  |  |
| 7 | compared to a level in a biological sample from the patient prior to, or earlier in, the   |  |  |
| 8 | therapeutic treatment, thereby monitoring the efficacy of the therapy.                     |  |  |
| 1 | 13. A method of monitoring the efficacy of a therapeutic treatment of                      |  |  |
| 2 | cancer, the method comprising the steps of:  |  |  |
| 3 | (i) providing a biological sample from a patient undergoing the therapeutic                |  |  |
| 4 | treatment; and   |  |  |
| 5 | (ii) detecting the level of methylation of the SOCS-3 promoter in the                      |  |  |
| 6 | biological sample compared to a level in a biological sample from the patient prior to, or |  |  |
| 7 | earlier in, the therapeutic treatment, thereby monitoring the efficacy of the therapy.     |  |  |
| 1 | 14. A method of screening for an agent that increases SOCS-3 activity, the                 |  |  |
| 2 | method comprising  |  |  |
| 3 | incubating a test compound with a cell comprising a SOCS-3 nucleic acid                    |  |  |
| 4 | having at least 80% identity to SEQ ID NO:1;   |  |  |
| 5 | selecting a compound that increases SOCS-3 activity, thereby identifying an                |  |  |
| 6 | agent that increases SOCS-3 activity.  |  |  |
| 1 | 15. The method of claim 14, wherein the SOCS-3 nucleic acid sequence                       |  |  |

further comprises a hypermethylated promoter.

2

WO 2005/023199 PCT/US2004/029037

| 1 | 16.  | The method of claim 15, further comprising a step of determining the  |  |
|---|--|---|--|
| 2 | amount of methylation of the SOCS-3 promoter following incubation with the test            |   |  |
| 3 | compound.  |   |  |
| 1 | 17.  | The method of claim 14, wherein the increase in SOCS-3 activity is    |  |
| 2 | determined by measuring the level of SOCS-3 mRNA transcript.                               |   |  |
|   |  |   |  |
| 1 | 18.  | The method of claim 14, wherein the increase in SOCS-3 activity is    |  |
| 2 | determined by measuring the level of SOCS-3 polypeptide.                                   |   |  |
| 1 | 19.  | A method of inhibiting proliferation of a cancer cell, the method     |  |
| 2 | comprising administering an agent that increases SOCS-3 activity to the cancer cell.       |   |  |
| 1 | 20.  | The method of claim 19, wherein the cancer cell has a hypermethylated |  |
| 2 | SOCS-3 promoter.   |   |  |
| 1 | 21.  | The method of claim 20, wherein the cancer cell is selected from the  |  |
| 2 |  | ·   |  |
|   | group consisting of a lung cancer cell, a breast cancer cell, a mesothelioma cell, a colon |   |  |
| 3 | cancer cell, and a sa  | ircoma cell.  |  |
| 1 | 22.  | The method of claim 19, wherein the agent is an expression vector     |  |
| 2 | encoding SOCS-3.   |   |  |
| 1 | 23.  | The method of claim 19, wherein the agent is recombinant SOCS-3.      |  |
| 1 | 24.  | The method of claim 19, wherein the agent is a demethylating agent.   |  |
| 1 | 25.  | A kit comprising methylation-specific primers that are selective for  |  |
| 2 | methylated residues present within the region from -1005 to -983 or from -754 to -737 of   |   |  |
| 3 | SEQ ID NO:3.   |   |  |